Supermediastinoscopies: A Step Forward in Lung Cancer Staging

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Clinical staging of lung cancer can be performed with different degrees of certainty. Sophisticated imaging techniques will better define the anatomical extension of the tumor compared with medical history, physical examination, and simple radiographic images. However, the highest certainty will be achieved using techniques that provide tissue confirmation of the anatomical extension of lung cancer into regional lymph nodes or adjacent structures. The Union Internationale Contre le Cancer recommends the use of the certainty (C) factor, which is an optional descriptor of the tumor, node, metastasis (TNM) classification that reflects the validity of classification according to the methods used (Table 1).[1]

The articles included in the mini-symposium of this issue aim at highest certainty in clinical staging of lung cancer, especially regarding nodal spread. In their article, De Leyn et al.[2] summarize 2 years' work undertaken by members of the European Society of Thoracic Surgeons who met in different workshops to review evidence on clinical, intraoperative, and pathological staging of non-small cell lung cancer. The resulting guidelines clearly show that the trend in Europe is toward avoiding approximation and aiming at the highest possible certainty. This implies tissue confirmation of regional nodal spread, except in a very selected group of patients with unusually small, peripheral squamous cell carcinomas with no evidence of nodal involvement on imaging or metabolic studies. Tissue confirmation also applies to restaging after induction treatment, when it is so important to assess objective response and rule out residual nodal disease to indicate further treatment. The European guidelines favor a thorough intraoperative nodal assessment and recommend systematic nodal dissection as the best way to evaluate hilar and mediastinal nodal spread. Both clinical and pathological staging have to be supported by an intense pathological study of the removed specimens: adequate specimen sampling and precise description of nodal involvement will complete the staging process and add to its certainty.

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The following four articles of the mini-symposium deal with variations of mediastinoscopy. In their own way, mediastinoscopic ultrasonography (MUS),[3] remediastinoscopy,[4] video-assisted mediastinoscopic lymphadenectomy (VAMLA),[5] and transcervical extended mediastinal lymphadenectomy (TEMLA)[6] are supermediastinoscopies that aim to improve the diagnostic accuracy of standard cervical mediastinoscopy.

Ultrasonography probes have been put into the pleural and abdominal cavities to identify small lung nodules and to assess liver metastases. It was a matter of time before they made it into the mediastinum. In their article, Hürtgen et al.[3] show how accurate MUS can be in ruling out direct mediastinal involvement by the primary lung cancer. In their series of 14 patients with cT4 tumors assessed by computed tomography who underwent resection, they found that none of them in fact had T4 tumors, and the correlation of MUS assessment and pathological staging after surgical intervention was almost perfect. Only one tumor was misclassified by MUS, but it was a T3 tumor, not a T4. Additionally, MUS predicted resectability in four additional patients who underwent thoracotomy but whose tumors were not resected because of functional or oncological reasons. MUS is a good example of how a combination of techniques (ultrasonography indicated on the basis of computed tomography findings and guided by mediastinoscopy) improves clinical staging.

Remediastinoscopy is a challenging operation that only experienced and dedicated surgeons enjoy performing, and they obtain the maximal yield from it. It is, indeed, a supermediastinoscopy: it demands skill, patience, and the conviction that the surgeon is doing something useful for the patient. In the era of induction therapy for locally advanced lung cancer, especially N2 disease, the persistence of mediastinal nodal involvement after induction has proved to be an ominous prognostic factor. Based on their own experience and on published reports on the subject, Van Schil et al.[4] show that remediastinoscopy is technically feasible, is no longer a contraindication for the established indications, and is more accurate than imaging studies when performed to assess tumor response after induction therapy. Remediastinoscopy for this indication also has prognostic relevance because it selects patients who will benefit most from lung resection. The authors are well aware that remediastinoscopy will be difficult to generalize because of its intrinsic technical difficulties because of peritracheal adhesions. They point out that both endobronchial and esophageal ultrasound-guided fine needle aspiration can be used for staging, reserving medias-

TABLE 1. Certainty (C) Factor and Its Applicability

Factor	Description of Staging Methods	Applicability
C1	Evidence from standard diagnostic means (e.g., inspection, palpation, and standard radiography, intraluminal endoscopy for tumors of certain organs)	
C2	Evidence obtained by special diagnostic means (e.g., radiographic imaging in special projections, tomography, computed tomography, ultrasonography, lymphography, angiography, scintigraphy, magnetic resonance imaging, positron emission tomography, endoscopy, biopsy, and cytology)	cTNM, rTNM, and ycTNM
C3	Evidence from surgical exploration, including biopsy and cytology	
C4	Evidence of the extent of the disease after definitive surgery and pathologic examination of the resected specimen	pTNM and ypTNM
C5	Evidence from autopsy	aTNM

cTNM, clinical tumor, node, metastasis classification; rTNM, pretreatment classification of recurrent tumors; ycTNM, classification after induction therapy before definitive treatment; pTNM, pathological classification; ypTNM, pathological classification after induction therapy; aTNM, autopsy classification.

tinoscopy for restaging. Both endoscopic techniques have also been used for restaging, with sensitivity and diagnostic accuracy values very similar to those of remediastinoscopy.[7,8] There is no doubt that the integration of these endoscopic techniques into the staging and restaging algorithms would make the whole process simpler with only a little loss of information provided by the more thorough exploration derived from surgical procedures. This integration is clearly favored by the European guidelines on staging and restaging.[2]

The last two articles of the mini-symposium deal with fascinating techniques, the objective of which is to perform mediastinal lymphadenectomy through the cervical incision used for mediastinoscopy. VAMLA[5] is a totally endoscopic technique performed through a video-mediastinoscope. TEMLA[6] is a mainly open procedure assisted with the video-mediastinoscope or video-thoracoscope at certain steps of the operation, i.e., when dissecting the subcarinal space or the subaortic region. With VAMLA, the nodal stations of the superior mediastinum, including right and left paratracheal and subcarinal nodes, are removed. The resection performed with TEMLA is more extensive because it also includes the highest mediastinal nodes, the subaortic and anterior mediastinal stations, and the paraesophageal nodes. Neither VAMLA nor TEMLA is indicated as the first staging procedure when there is evident mediastinal involvement, in which case endoscopic procedures with fine needle aspiration would be the first choice. An important aspect of these techniques is that they remove all the lymph nodes of the explored nodal stations, thus facilitating the identification of minimal nodal disease that is not identified on computed tomography or positron emission tomography and that escapes standard mediastinoscopy. This complete removal is an advantage but, at the same time, poses an important problem: for patients with N2 disease diagnosed by VAMLA or TEMLA who receive induction therapy, there are no nodes left to assess objective tumor response and downstaging. We know that nodal status after induction is an important prognostic factor, but for patients undergoing VAMLA and TEMLA, nodal restaging is not possible because there is no material left for a new biopsy. New parameters of tumor response based on the T component of the TNM classification or on biologic factors will have to be determined to indicate further therapy after induction. VAMLA and TEMLA could also be considered part of the induction treatment because, for patients with mediastinal nodal disease, the tumor is both staged and down-staged by the operations. One is tempted to think that, in this circumstance, if there has been no progressive disease during induction therapy, the patient deserves to be offered the benefit of resection, especially when the intraoperative pathologic study of the remaining lymph node specimen removed at thoracotomy confirms the absence of nodal involvement, and the required resection is a lobectomy.

Fifty years after Carlens performed his first mediastinoscopy, technical improvements have allowed the development of the procedure to such an extent that it barely resembles the original one. European thoracic surgeons are for the highest staging certainty, and this implies the use of mediastinoscopy. Remediastinoscopy has already meant a change in paradigms, allowing the selective indication of lung resection after induction therapy. It is not difficult to envisage new paradigm changes in clinical practice based on the results of VAMLA and TEMLA. Professionals involved in the care of patients with lung cancer should have their minds open to absorb all these changes and make the best use of them.

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